

Assessment of Propofol Usefulness as an Anesthetic Agent During Colonoscopy

MR Ghadir¹, MH Pishvaei², A Shafaghi³, F Joukar³, F Khatib¹, F Mansour-Ghanaei^{3*}

1. Department of Gastroenterology and Hepatology, Qom University of Medical Sciences, Qom, Iran
2. Department of Anesthesiology, Hazrat-e-Masoumeh (PBUH) Hospital, Qom University of Medical Sciences, Qom, Iran
3. Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences, Rasht, Iran

***Corresponding Author:**

Fariborz Mansour-Ghanaei, MD
Professor of Gastroenterology and Hepatology, Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences, Razi Hospital, Sardar-Jangle Ave., Rasht 41448-95655, Guilan, Iran.
Tel: +98 131 5535116
Fax: +98 131 5534951
E-mail: ghanaei@gums.ac.ir
Received: 11 Nov. 2010
Accepted: 10 Jan. 2011

ABSTRACT

BACKGROUND

Propofol is used as a sedative drug during colonoscopy. In this study we analyzed the adverse effects of propofol (i.e., hemodynamic and respiratory) on patients who underwent colonoscopies.

METHODS

This study was performed in Qom Province, Iran. In this study, 125 patients (63 females, 62 males) were enrolled. Study patients were administered (0.5-1.5 mg/kg) intravenous propofol by an anesthesiologist.

Oxygen saturation and blood pressure were recorded at three minute intervals. We used the American Society of Anesthesiology (ASA) classification to stratify patients by risk prior to the procedure. For statistical analysis, the chi-square and paired t-tests were used. A *p*-value less than 0.05 was considered significant.

RESULTS

Patients' mean age was 45.36 ± 16.19 years. ASA-I comprised 25.6% of study patients and 74.4% were categorized as ASA-II. Hypopnea occurred in 56.8% of patients and was prolonged in 32.4%. Of the study patients, 5.6% developed hypoxemia which was successfully controlled by the administration of nasal oxygen and no need for mechanical ventilation. The mean arterial blood pressure ($p < 0.0001$), oxygen saturation ($p < 0.0001$) and heart rate ($p < 0.0001$) significantly decreased during colonoscopy. The occurrence of hypopnea significantly increased in patients with pre-procedure oxygen saturation levels $\leq 95\%$ ($p < 0.02$), age ≥ 50 years ($p < 0.0001$) and ASA class II ($p < 0.0001$). Agitation, hypotension and cough were seen in 1.6%, 1.6% and 0.8% of patients, respectively.

CONCLUSION

Propofol has a short half life that enables faster recovery of normal neurologic and social functions we recommend the use of propofol under supervision of anesthesiologist or a trained gastroenterologist.

KEYWORDS

Propofol; Conscious sedation; Colonoscopy; Adverse effect

INTRODUCTION

Propofol is an intravenously administered hypnotic agent initially used for the induction and maintenance of appropriate sedative conditions. This drug offers some potential advantages as a sedative agent which include faster onset of sedation, faster patient recovery, better post procedure patient functioning and better patient satisfaction.^{1,2}

Comfort during colonoscopy is an important condition for the patient to accept repeated procedures, thus the endoscopy community should collectively seek out solutions to the high cost of anesthetist-delivered sedation for endoscopy.

Propofol is increasingly used for sedation during colonoscopy, with many recent reports of randomized controlled trials and large non-randomized case series. It can lead to faster recovery and discharge times without an increase in side-effects.³

A number of programs have demonstrated that specifically trained registered nurses under the direction of trained endoscopists can administer propofol safely for endoscopic procedures without the direct involvement of an anesthetist or anesthesiologist.⁴⁻¹⁰

The American Gastroenterological Association (AGA) and two other professional societies issued a joint statement in March 2004 endorsing the use of propofol for endoscopy sedation by adequately trained endoscopists and endoscopy nurses.¹¹ This position was reinforced in 2007 when the AGA released a review of endoscopic sedations which also addressed the medico-legal considerations associated with propofol use.¹² Another newer guideline published in 2010 was evidence and consensus based. This guideline resulted from a collaborative effort from representatives of the European Society of Gastrointestinal Endoscopy (ESGE), the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA), and the European Society of Anesthesiology (ESA). This guideline is a comprehensive frame work on how to implement and practice non-anesthesiologist-administered propofol (NAAP).¹³

Propofol can indeed induce very serious respiratory depression and its use by non-anesthesiologists must occur only after specific training. Administration by anesthetists is associated with the cost of their professional fees; which increase in total cost, reduces the competitiveness of endoscopy relevant to other diagnostic procedures.

The purpose of this study was to analyze the side effects of propofol, including hemodynamic and respiratory effects, on patients undergoing colonoscopy and thus assess its usefulness for sedation during colonoscopy.

MATERIALS AND METHODS

The study was designed by the Gastrointestinal and Liver Disease Research Center (GLDRC), Guilan Province, Iran and performed in the Gastroenterology Department at Hazrat-e-Masoumeh (PBUH) Hospital, Qom, Iran. It was approved by the Ethics Committee of GLDRC and written informed consent was obtained from each patient.

We analyzed 125 patients (63 women and 62 men) who were admitted for a same day colonoscopy procedure. All patients had an indication for colonoscopy. None of the patients had a history of drug sensitivity reactions or proven cardiovascular risk. This study was conducted prospectively over a fifteen month period from March first 2007 to June first 2008. We used the American Society of Anesthesiology Classification System (ASA grading I-IV) to stratify patients by risk prior to procedure. ASA grading includes:

ASA grade I:

Healthy patient with no medical problems

ASA grade II:

Mild systemic disease

ASA grade III:

Severe systemic disease but not incapacitating

ASA grade IV:

Severe systemic disease that is life-threatening.¹⁴

Patients were given an intravenous propofol (Diprivan, Astra Zeneca, USA) bolus (0.5-1.5 mg/kg) by an anesthesiologist.

The required drug dose was determined by the anesthesiologist according to patient characteristics such as age, weight and duration of procedure. If necessary, an additional bolus injection was administered. Oxygen saturation and heart rate were monitored by pulse oximetry and blood pressure was recorded by automated sphygmomanometry at three minute intervals. During the procedure, patients who exhibited shallow breathing for longer than 30 sec (prolonged hypopnea) were administered supplemental oxygen at a rate of 2 l/min by nasal cannula. After completion of the procedure, patients were transferred to a recovery room and were closely observed for 30 min. The chi-square test for statistical analysis of qualitative data was used. The paired t-test was used to test differences between pairs of measured values before and during the procedure. A p -value < 0.05 was considered significant.

RESULTS

Study participants consisted of 63 (50.4%) women and 62 (49.6%) men. The mean age of patients was 45.36 ± 16.19 years. There were 32 (25.6%) patients in ASA-I (healthy patients) and 93 (74.4%) classified as ASA-II (patients with disease of one body system).

None of the study patients were in ASA groups III or IV. An episode of hypopnea occurred in 71 (56.8%) of patients that was prolonged in 32.4%, but transient in others. The mean time of hypopnea was 33.84 ± 18.41 sec. Of the patients, 5.6% developed hypoxemia. All hypoxemia episodes were successfully controlled by the administration of nasal oxygen without the need for mechanical ventilation. Mean arterial blood pressure, oxygen saturation and heart rate were significantly decreased during the colonoscopy (Table 1). The occurrence of hypopnea was significantly increased

in patients with a pre-procedure oxygen saturation $\leq 95\%$, age ≥ 50 years and ASA-II (Table 2).

Table 1: Comparison of parameters before and during colonoscopy.

Parameter	BC	DC
SBP (mmHg)	130.9 ± 15.9	109.5 ± 15.1^a
DBP (mmHg)	79 ± 11.5	69.8 ± 9.7^a
HR (beat/min)	78.3 ± 11.3	71.6 ± 10.9^a
O ₂ sat (%)	96.8 ± 1.5	95.6 ± 2.2^a

Comparison of systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and oxygen saturation (O₂sat) before colonoscopy (BC) and during colonoscopy. Data were presented as mean \pm SD. a denotes significant ($p < 0.0001$) difference between parameters before and during colonoscopy.

Table 2: Comparison of some parameters between patients with and without an episode of hypopnea.

Condition Parameters	Patients without hypopnea n (%)	Patients with hypopnea n (%)
Sex ratio ($\frac{M}{F}$)	$\frac{25}{29}$	$\frac{37}{34}$
Age > 50 years	9 (20)	36 (80) ^b
ASA class II	30 (32.3)	63 (97.75) ^b
Pre-procedure O ₂ sat $\leq 95\%$	3 (16.7)	15 (83.3) ^c

Comparison of sex ratio ($\frac{M}{F}$), age > 50 years, American Society of Anesthesiology (ASA) class II and pre-procedure oxygen saturation (O₂ sat) $\leq 95\%$ between patients without hypopnea (-ve) and patients with hypopnea (+ve). Data were presented as number of samples and percent n (%). b denotes significant difference between age > 50 years, ASA class II between (-ve) and (+ve). c denotes significant ($p < 0.02$) difference between pre-procedure O₂ sat $\leq 95\%$ between (-ve) and (+ve).

No complications were related to the colonoscopy procedure. Patients' median recovery time was 8 min (range 3-18 min) and no serious respiratory or hemodynamic complications were noted. Agitation occurred in 2 (1.6%) patients and cough was reported in 1 (0.8%) patient. Hypotension, defined as a systolic blood pressure below 80 mmHg was recorded in 2 (1.6%) patients who were given a normal saline bolus by the attending anesthesiologist. Bradycardia, defined as a heart rate less than 50 beats/min was noted in 2 (1.6%) patients and treated with 1mg atropine.

DISCUSSION

Sedation during colonoscopy seems to be essential in order to ensure patient comfort and a high quality examination. Sedation can increase

tolerance by the patients for a second colonoscopy, when required. The problem of colon cancer is raising more and more interest in the gastroenterological world due to the increasing number of diagnosed cases and the high mortality induced by this disease. As a consequence, new strategies should be developed in our country in order to diagnose colorectal cancers in its early stages. We believe that a national consensus regarding sedation during colonoscopy should be reached, thus ensuring a high standard of quality and safety during this procedure.

The choice of sedative in gastroenterology is operator dependent but generally consists of benzodiazepines used either alone or in combination with an opiate.^{15,16} Such combination may increase the risk of oxygen desaturation and cardiopulmonary complications¹⁷ because sedation is a continuum; it is not always possible to predict how individual patients will respond. Due to the potential for rapid, profound changes in sedative/anesthetic depth to maintain immobility and unconsciousness during the procedure, our choice of agent is propofol.

In this study hypopnea, in particular transient hypopnea, was seen in a significant number of patients. This adverse effect was treated with oxygen administration with no need for mechanical ventilation. A recent meta-analysis found no increase in the risk of cardiopulmonary complications with the use of propofol sedation for endoscopy compared with the use of traditional sedative agents.¹⁸ Age above 50 and high ASA class were two important parameters for the occurrence of cardiopulmonary complications ($p < 0.0001$ for both). We believed that appropriate patient selection is critical due to a more recent study that has reported a small number of deaths in patients with a high ASA class who received propofol during interventional procedures.¹⁹ In our study, blood pressure, heart rate and oxygen saturation decreased significantly during colo-

noscopy. Significant hypotension and bradycardia were seen in a small number of patients. Monitoring of cardiopulmonary function during this procedure is of utmost importance thus allowing for a significant reduction in morbidity and mortality. Gasparovic et al.²⁰ reported 2.4% and Kulling et al.²¹ reported a 3.7% oxygen desaturation with the use of propofol. We prevented hypoxemia with the administration of supplementary oxygen at a rate of 2 L/min. One study has reported desaturation in 40% of patients (Table 3).²²⁻²³

During the administration of propofol; patients should be monitored without interruption to assess level of consciousness and identify early signs of hypotension, bradycardia, apnea, airway obstruction and/or oxygen desaturation. Ventilation, oxygen saturation, heart rate and blood pressure should be monitored at regular and frequent intervals. Monitoring for the presence of exhaled carbon dioxide should be utilized when possible, since movement of the chest will not dependably identify airway obstruction or apnea. It is important to note that propofol may cause vasodilation and myocardial depression independent of hypoxia and hypoventilation. While technology exists for capnography, the current literature does not support such a routine because no change in clinical outcome has been documented.¹²

Propofol has a shorter time to recovery and, hence, earlier discharge from the endoscopy unit. Patients who receive propofol (half-life: 2-4 min) as a single agent recover normal neurological and social functions significantly quicker than benzodiazepines (half-life: 30 min) and/or narcotics (half life: 3-4 h). The median recovery time was 8 min in our study. A quicker onset of action and less patient discomfort, both of which benefit the endoscopist and the patients is seen with propofol.^{1,2,24}

Bronchospasm, burning in the throat, cough and hiccoughs were rare respiratory complications of propofol. However each occurred in

Table 3: Comparison of the frequency of two main complications of propofol use between recent studies and this study.

References	Number of patients	Procedure	Hypoxemia (%)	Hypotension (%)
Qadeer et al. 2005	1161	Endoscopy (EGD) Colonoscopy (ERCP) Colonoscopy	8.8	2.8
McQuaid & Laine 2008	3918	EGD Colonoscopy	11	5
Singh et al. 2008	1181	Colonoscopy	5.4	12.5
This study	125	Colonoscopy	5.6	1.6

EGD: Esophagogastroduodenoscopy

ERCP: Endoscopic retrograde cholangiopancreatography

less than 1% of patients, as in our study only one patient had a cough. Cough reflex is the main mechanism of airway defense by protecting the lungs from aspiration and clearing the airways from retained secretions. However, residual concentration of anesthesia and residual sedation observed after anesthesia may depress this reflex.²⁵ Fortunately, residual sedation after propofol anesthesia for colonoscopy dose not adversely affect cough reflex.²⁶

Agitation was seen in 0.8% of our patients. Paradoxical reactions including hyperactive or aggressive behavior have been reported.¹⁷ Anesthetic agents such as propofol are reserved for patients who remain uncooperative on standard regiments or who are perceived to be at high risk for agitation unless a deeper level of sedation is achieved.^{27,28}

According to our findings, we recommend that endoscopists seeking to use propofol in their practice should undergo certification in advanced cardiac life support and a formal course of instruction with an individual (such as an anesthesiologist) who is familiar with propofol use. The only rationale for anesthesiologists to not deliver propofol for endoscopy would be the high cost associated with practice. Although the FDA essentially never confines the use of a drug to a given specialty, we believe that one must be an anesthesiologist or nurse anesthetist to use this drug, as in our study. This study has shown that the use of propofol for sedation during colonoscopy can lead to an acceptable sedation without any increase in side effects. Although sedation involves a risk of heart or lung problems which rarely may be fatal, rescue of a patient from a

deeper level of sedation is an intervention by a practitioner proficient in airway management and advanced life support. Gastroenterologists themselves should not use propofol without diligent monitoring by anesthetists. We recommend using propofol in the case of gastroenterologists who have undergone continuing education in its use, under anesthesiologist supervision or for non anesthesiologists who are trained in propofol administration.

ACKNOWLEDGMENTS

We thank Dr. Sepiedeh Besharati for preparation of the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Sipe BW, Rex DK, Latinovich D, Overley C, Kinser K, Bratcher L, et al. Propofol versus midazolam/meperidine for outpatient colonoscopy: administration by nurses supervised by endoscopists. *Gastrointest Endosc* 2002;**55**:815-25.
2. Ulmer BJ, Hansen JJ, Overley CA, Symms MR, Chadala-wada V, Liangpunsakul S, et al. Propofol versus midazolam/fentanyl for outpatient colonoscopy: administration by nurses supervised by endoscopists. *Clin Gastroenterol Hepatol* 2003;**1**:425-32.
3. Singh H, Poluha W, Cheung M, Choptain N, Baron KI, Taback SP. Propofol for sedation during colonoscopy. *Cochrane Database Syst Rev* 2008;**4**:CD006268.
4. Gonzalez-Huix F, Aldeguez X, Fort E, Salinas E, Figa M, Hombrados M, et al. Sedation without anesthesiologist in 5250 endoscopic procedures: midazolam vs. midazolam+dolantine vs. propofol. *Gastrointest Endosc* 2004;**59**:AB133.
5. Külling D, Rothenbühler R, Inauen W. Safety of nonanesthetist sedation with propofol for outpatient colonoscopy and esophagogastroduodenoscopy.

- Endoscopy* 2003;**35**:679-82.
6. Cohen LB, Hightower CD, Wood DA, Miller KM, Aisenberg J. Moderate level sedation during endoscopy: a prospective study using low-dose propofol, meperidine/fentanyl, and midazolam. *Gastrointest Endosc* 2004;**59**:795-803.
 7. Vargo JJ, Eisen GM, Faigel DO, Holub J, Lieberman DA. Cardiopulmonary complications with non-anesthesiologist-administered propofol vs. standard sedation: The CORI experience. *Gastrointest Endosc* 2005;**59**:AB132.
 8. Koshy G, Nair S, Norkus EP, Hertan HI, Pitchumoni CS. Propofol versus midazolam and meperidine for conscious sedation in GI endoscopy. *Am J Gastroenterol* 2000;**95**:1476-9.
 9. Yusoff IF, Raymond G, Sahai AV. Endoscopist administered propofol for upper-GI EUS is safe and effective: a prospective study in 500 patients. *Gastrointest Endosc* 2004;**60**:356-60.
 10. Rex DK, Heuss LT, Walker JA. Nurse administered propofol sedation: safety record among individual nurses and physicians in 3 centers. *Am J Gastroenterol* 2004;**99**:S300.
 11. Recommendations on the administration of sedation for the performance of endoscopic procedures. A joint statement of a working group from the American College of Gastroenterology (ACG), The American Gastroenterological Association (AGA) and the American Society for Gastrointestinal Endoscopy (ASGE); 2008. [Available at: <<http://www.gastro.org/wmspage.cfm?parm1=371>>(Version current at March 3,2008).]
 12. Cohen LB, Delegge MH, Aisenberg J, Brill JV, Inadomi JM, Kochman ML, et al. AGA Institute review of endoscopic sedation. *Gastroenterology* 2007;**133**:675-701.
 13. Dumonceau JM, Riphaus A, Aparicio JR, Beilenhoff U, Knappe JT, Ortmann M, et al. European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology Guideline: Non-anesthesiologist administration of propofol for GI endoscopy. *Endoscopy* 2010;**42**:960-74.
 14. Sanjay P, Jones P, Woodward A. Inguinal hernia repair: are ASA grades 3 and 4 patients suitable for day case hernia repair? *Hernia* 2006;**10**:299-302.
 15. Zakko SF, Seifert HA, Gross JB. A comparison of midazolam and diazepam for conscious sedation during colonoscopy in a prospective double-blind study. *Gastrointest Endosc* 1999;**49**:684-9.
 16. Ristikankare M, Hartikainen J, Heikkinen M, Janatuinen E, Julkunen R. Is routinely given conscious sedation of benefit during colonoscopy? *Gastrointest Endosc* 1999;**49**:566-72.
 17. Waring JP, Baron TH, Hirota WK, Goldstein JL, Jacobson BC, Leighton JA, et al. Guidelines for conscious sedation and monitoring during gastrointestinal endoscopy. *Gastrointest Endosc* 2003;**58**:317-22.
 18. Qadeer MA, Vargo JJ, Khandwala F, Lopez R, Zuccaro G. Propofol versus traditional sedative agents for gastrointestinal endoscopy: a meta-analysis. *Clin Gastroenterol Hepatol* 2005;**3**:1049-56.
 19. Wehrmann T, Riphaus A. Sedation with propofol for interventional endoscopic procedures: a risk factor analysis. *Scand J Gastroenterol* 2008;**43**:368-74.
 20. Gasparović S, Rustemović N, Opacić M, Premuzić M, Korusić A, Božikov J, et al. Clinical analysis of propofol deep sedation for 1,104 patients undergoing gastrointestinal endoscopic procedures: a three year prospective study. *World J Gastroenterol* 2006;**12**:327-30.
 21. Külling D, Rothenbühler R, Inauen W. Safety of non-anesthetist sedation with propofol for outpatient colonoscopy and esophagogastroduodenoscopy. *Endoscopy* 2003;**35**:679-82.
 22. Holm C, Rosenberg J. Pulse oximetry and supplemental oxygen during gastrointestinal endoscopy: a critical review. *Endoscopy* 1996;**28**:703-11.
 23. McQuaid KR, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. *Gastrointest Endosc* 2008;**67**:910-23.
 24. Ng JM, Kong CF, Nyam D. Patient-controlled sedation with propofol for colonoscopy. *Gastrointest Endosc* 2001;**54**:8-13.
 25. Tagaito Y, Isono S, Nishino T. Upper airway reflexes during a combination of propofol and fentanyl anesthesia. *Anesthesiology* 1998;**88**:1459-66.
 26. Guglielminotti J, Rackelboom T, Tesnière A, Panhard X, Mentre F, Bonay M, et al. Assessment of the cough reflex after propofol anaesthesia for colonoscopy. *Br J Anaesth* 2005;**95**:406-9.
 27. Kaddu R, Bhattacharya D, Metriyakool K, Thomas R, Tolia V. Propofol compared with general anesthesia for pediatric GI endoscopy: is propofol better? *Gastrointest Endosc* 2002;**55**:27-32.
 28. Theodorou T, Hales P, Gillespie P, Robertson B. Total intravenous versus inhalational anaesthesia for colonoscopy: a prospective study of clinical recovery and psychomotor function. *Anaesth Intensive Care* 2001;**29**:124-36.